UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/073,521	02/11/2002	Wen-Fu T. Lai	10627-004001	5316

26161 7590 03/15/2004

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
NAFF, DAVID M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,521	LAI ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,6,7,9-12,16,17 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7 & 10* is/are allowed.

6)☒ Claim(s) *1,2,6,9,11,12,16,17 and 21-24* is/are rejected.

7)☒ Claim(s) *7 and 10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

The amendment of 1/9/04 amended claims 1, 2, 7, 10-12, 16, 17, and 23, and canceled claims 3-5, 8, 13-15, 18-20 and 22.

Claims examined on the merits are 1, 2, 6, 7, 9-12, 16, 17 and 21-24 which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 1, 2, 6, 9, 11, 12, 16, 17 and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lai (5,876,444) in view of Muller et al (6,623,963 B1) and Mansmann (6,530,956 B1) for reasons in the previous office action of 10/6/03 and for reasons herein.

The claims are drawn to producing a cartilage implant by embedding chondrocytes or mesenchymal stem cells in a three-dimensional substrate containing randomly rewound α-helical monomers from partially digested type I collagen, and growing the chondrocytes or mesenchymal stem cells in the substrate to produce the implant. In dependent claims, the substrate also contains randomly rewound α-helical monomers from partially digested type II collagen. Also claimed is the resulting implant.

Lai discloses producing a reconstituted collagen template for implanting to articular wounds to facilitate regeneration of chondrocytes and extracellular matrix. The collagen template is prepared by uncoiling of the triple-helix structure of type I collagen

using a proteolytic enzyme to produce α-helix monomers, reducing disulfide bonds to -SH groups with mercaptoethanol and crosslinking the α-helical monomers with glutaraldehyde (col 2, lines 26-32, col 4, lines 5-15, and Schemes I-III (cols 6 and 7)).

Muller et al disclose a cellular matrix for implanting to repair tissue. The implant contains a reconstituted type II collagen that has been produced by a method that involves partial digestion (Example I) with a proteolytic enzyme to break crosslinking of the collagen in its telopeptide region into its virtually non-crosslinked, atelocollagen, triple helix form (col 4, lines 44-46). The collagen is then reconstituted to provide sufficient structural stability for use as a scaffold by imparting crosslinking in the collagen (col 4, lines 47-50 and col 5, lines 5-9). Crosslinking can be accomplished with chemical compounds (col 5, lines 48-56) or by heating or using radiation (col 5, lines 57-60). Chondrocytes are grown on the matrix, and adhere firmly or integrate into the matrix (col 9, lines 25-26). Type II collagen provides a natural environment for cell growth since it is a scaffolding for chondrocytes *in vivo* (col 9, lines 11-15).

Mansmann discloses a scaffold having compartments that are filled with a matrix material that may be formed of collagen that promotes rapid cell growth and cartilage secretion (col 8, lines 25-48), and contains seeded cells such as chondrocytes. The cells may be in a paste that is injected into the compartments (col 16, lines 1-22).

It would have been obvious to seed the collagen implant of Lai with chondrocytes as suggested by Muller et al and Mansmann disclosing seeding collagen implants with chondrocytes prior to implanting. Seeding with the cells would have been expected to provide cells present when implanted to produce repair tissue sooner. Cells integrated into the collagen matrix as disclosed by Muller et al (col 9, line 25) would be embedded in the matrix. It would have been apparent from Muller et al that reconstituting can result from the atelocollagen form of collagen reestablishing its crosslinking between variable regions along the collagen molecule to form a more rigid structural integrity to provide a scaffold (col 4, lines 44-54), and that this can be accomplished without the use of glutaraldehyde (col 5, lines 57-65). It would have been obvious to use the alternative method of crosslinking suggested by Muller at al in place of using glutaraldehyde as disclosed by Lai since it is apparent from Muller et al that either crosslinking procedure will result in a structural integrity sufficient to provide a scaffold. It would have been further obvious to combine the type II collagen of Muller et al with the type I of Lai et al, as in dependent claims such as 2, to obtain the properties of both together, and to obtain the property of type II collagen providing an environment similar to that *in vivo* as disclosed by Muller et al (col 9, lines 13-15). The method of producing the type II collagen of Muller et al results in randomly rewound α-helical monomers of type II collagen. Obtaining the collagens and cells from different animal sources as in claims 6, 9, 21, 23 and 24 would have

been obvious since Muller et al and Mansmann use different animal sources for the cells and collagen.

Response to Arguments

Applicant's arguments filed 1/9/04 have been fully considered but they are not persuasive.

Applicants urge that crosslinking with glutaraldehyde as disclosed by Lai produces a polymer, and does not result in a substrate made of α-helical type I collagen monomers. However, the present specification discloses (page 5, line 21) a mixture of types I and II collagens monomers becoming polymerized. The polymerized mixture is a polymer resulting from rewinding, and crosslinking occurs during polymerizing as disclosed by Muller et al when reconstituting without the use of glutaraldehyde. After polymerizing as disclosed in the specification, the monomers per se no longer exist since they have polymerized. As set forth above, it would have been obvious to crosslink in Lai without the use of glutaraldehyde. Moreover, random rewinding can occur in Lai even when glutaraldehyde is used due to crosslinking between variable regions along the collagen molecule as disclosed by Muller et al, and due to the -SH groups reforming disulfide bonds. There is inadequate evidence to establish that crosslinking with glutaraldehyde prevents random rewinding in the process of Lai. The present claims do not exclude the use of glutaraldehyde or other chemical crosslinking agent.

Claims 7 and 10 are allowable, but are objected to as being dependent on a rejected claim.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
3/12/04